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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,823	06/26/2001	John R. Neefe	12071-003001	2643

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1648	12

DATE MAILED: 10/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/891,823	Neefe et al
Examiner	**Art Unit**
A. R. SALMI	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *9/18/2002; 9/10/2002; 9/3/2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above, claim(s) *14-35* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 7*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-35 are pending.

Raw Sequence Listing have been entered.

Submitted Information Disclosure Statement (I.D.S) is noted.

Election/Restriction

Applicant's election without traverse of Group I (claims 1-13) in Paper No. 9 is acknowledged. Claims 14-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups. Election was made without traverse in Paper No. 9. Claims 1-13 are considered.

Applicants are reminded to cancel the claims to the non elected claims.

Claim Rejections - 35 USC § 112

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for recitation of "suspected of having a wart", the said term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite for suspecting a subject having a wart, and one of ordinary skill in the art would not be reasonably

apprised of the scope of the invention. In addition, the intended heat shock protein is/are not defined. Moreover, the intended "immunostimulatory fragment thereof" are not defined, what are these fragments? Is TNF intended? Moreover, isn't the heat shock protein "immunostimulatory' molecule? It appears Applicants use redundant terms. Please clarify the difference between the heat sock and the immunostimulatory fragments. Still further, the intended HPV protein or an antigenic fragments are not defined, is three amino acid long HPV intended? Is E4 intended? In addition, the intended sufficient amount is not defined. The "amount sufficient' is a relative term, to practice the method one should know what amount or range is needed. This affects the dependent claims.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the hsp protein type which would be suited to treat HPV, the HPV protein, the "fragment, the amount.

Claim Rejections - 35 USC § 112

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing immune response utilizing Hsp65 heat shock proteins complexed with E7 protein of human papillomavirus (HPV) does not reasonably provide enablement for method of any and all types of epitopes of any and all human papillomavirus proteins whether it be early or late proteins complexed with any and all heat shock proteins to

induce an immune response absent inducing severe adverse effect. Nor the specification sets any disclosure for teaching of any and all fusion proteins of HPV proteins and immunostimulatory fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The specification does not set forth an adequate teaching for the broad scope of the claimed invention, in order to enable the full scope of the method one needs products that would actually enable the process. In addition, applicants are reminded that this field is highly unpredictable and absent adequate teaching by the applicants' disclosure one of ordinary skill in the art would be required to conduct large quantity of experimentation to enable the full scope of the claimed invention. Applicants' own teaching is a testament to the unpredictability of field. The whole host of epitopes and heat shock proteins would not induce the desired response. For instance, the immune response might be targeted towards the heat shock protein rather than the epitope, to find the appropriate heat shock protein, immunostimualtory molecule, or fragments thereof undue experimentation would be required. In addition, the specific epitopes should be taught. The claims currently are broadly reciting any epitope from HPV, but it is not clear whether the epitopes are from a structural protein or non-structural proteins, whether they would induce type I or type II response, or whether or not the heat shock would be a proper chaperoned to the peptide. There is no teaching whether or not the auto-immune response would result, which absent teaching undue experimentation would be required to practice the invention. Not all early proteins are viable proteins to induce immune response as evidence see Lin et al (Journal of

Virology, 1993, 67 (1), pp. 382-389) where it is taught that upon administration of E4 or E5 no antibodies were detected. Applicants have general statements regarding the method to induce an immune response with heat shock protein and HPV complexed. Applicants have utilized a well known early protein E7, i.e HPV16 E7, which is well known in the art as a viable antigen for inducing immune response. However, the results from E7 cannot be extrapolated to any and all early papillomavirus proteins. In addition, with regard to an unpredictable field, this does not constitute an adequate disclosure. See Fiers v. Revel (25USPQ2d 1601 at 1606; and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001-1007). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision). In the instant case the specification does not teach or provide any guidance for development of a broad complex of all epitopes and all heat shock proteins as recited above. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation. The applicants can not rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant disclosure, the applicants have not disclosed a method of inducing immune response with any and all heat shock proteins or immunostimulatory fragments. The specification does not set forth the metes and bounds of multiple myriads of complexed proteins which can be employed in a method, there is not enough information about it in literature either to guide the one of ordinary skill in the art to predict the undisclosed regions where the region may encompass, and/or predict the complex of any and all epitope with any and all heat shock protein. Therefore, since applicants were not in possession of material that can be used in a method, as a consequence the written description of invention is lacking. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter

alia that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art ... to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other

> materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Mizzen et al (WO 99/07860).

The claims are directed to a method of treating human papilloma virus tumors by a complex formed by fusing human papillomavirus protein and heat shock protein. In addition, the claims are directed to utilization of fusion protein of Hsp60 or Hsp 70 fused to HPV E7 proteins. The teaching and claims of the above cited patent clearly meets and anticipates the claimed invention. Mizzen et al taught the composition of heat shock proteins fused to E7 proteins of human papillomavirus and method of utilizing the said proteins in treating and inducing immune response (see the abstract, and all the claims). In

addition, the teaching of the Mizeen et al meets the broad range recitation of fusion composition (see page 22, lines 14-29).

Claims 1-4, 6-13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chu et al (FASEB Journal, March 20, 1998, 12 (5): A909).

The disclosure of the above cited abstract meets the broad limitations of the claimed invention. Chu et al taught the fusion of Hsp65 and E7 protein of human papillomavirus would induce therapeutic effect. Regarding the modification of using composition titers within the broad recited range is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233.

Claims 1, 8-13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Whittle et al (WO 98/04706).

The teaching and claims of the above cited world patent meets the broad recitation of the claims. Whittle et al taught the fusion papillomaviruses combined with immunostimulatory molecules (see page 9, lines 28-34). In addition, the broad range of protein concentration is also anticipated by the above cited patent (see claims 8-10)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 6-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhou G (Chinese Patent No. CN1248631A, March 2000).

The disclosure and claims of the above cited Chinese patent meets the claimed invention (see the entire abstract, and claims 1, 4). It is noted that applicants have provided the abstract of the above cited patent to the Office. The abstract does not indicate the limitations of the Hsp65 fusion with E7 protein of papillomavirus, and does not fully disclose the full breath of Zhou's invention. However, upon examination of the entire patent of Zhou, ones gets a better idea of the full scope of the his invention. The patent is in Chinese, the examiner has utilized the resources available to the patent Office by obtaining a standby translation of the said patent, and has come to the conclusion that Zhou's patent indeed anticipates the now claimed invention. A copy of the said Chinese patent will accompany this office Action. Regarding the modification of using composition titers within the broad recited range is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) because

it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233.

Claims 1-3, 5-13 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Chen et al, Cancer research, Feb., 2000, vol. 60, pp. 1035-1042.

Chen et al taught a fusion of heat shock protein of Hsp70, and papillomavirus E7 protein genes can be utilized in treating human papillomavirus (see the abstract). Applicants are reminded that upon administration of the fusion genes the translated proteins at the cellular milieu are responsible for induction of immune response and not the genes. Hence the product and method of utilizing the product inherently do what the applicants invention is intent to accomplish. The burden is on the applicants to show that such is not case.

Claims 1-3, 5-13 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Liu et al, Journal of Virology, Mar. 2000, Vol. 74, No. 6, pp. 2888-2894.

Li et al taught a fusion of heat shock protein of Hsp70, and papillomavirus E7 protein genes can be utilized in treating human papillomavirus (see page 2889, left

column, 1st full paragraph). Applicants are reminded that upon administration of the fusion genes the translated proteins at the cellular milieu are responsible for induction of immune response and not the genes. Hence the product and method of utilizing the product inherently do what the applicants invention is intent to accomplish. The burden is on the applicants to show that such is not case.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

10/14/2002

ALI R. SALIMI
PRIMARY EXAMINER